

REMARKS

Claims 1-4, 6-14, 16, 19, 21, 23-26, 30-40, 56-68, 82 and 103-156 were pending in the application. Claims 1, 19, 21, 82, 149, 150 and 154 have been amended. Therefore, claims 1-4, 6-14, 16, 19, 21, 23-26, 30-40, 56-68, 82 and 103-156 are currently pending in the application.

No new matter has been added. The claims have been amended to clarify the invention.

Amendments to the claims should in no way be construed as acquiescence to any of the Examiner's objections and/or rejections. The amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The amendments to the claims are not related to any issues of patentability.

Applicants note with appreciation that claims 25, 26, 56-68 and 103-108 were found to be free of the prior art.

Rejection of Claims 1-4, 6-14, 16, 19, 21, 23, 24, 30-40, 82 and 140-154 under the Judicially Created Doctrine of Obviousness-Type Double Patenting

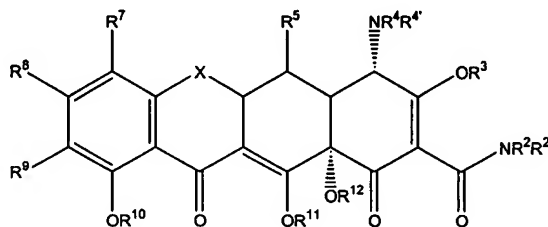
Claims 1-4, 6-14, 16, 19, 21, 23, 24, 30-40, 82 and 140-154 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 26-54 of co pending Application No. 10/839,023.

While in no way admitting that the present claims are obvious over claims 1 and 26-54 of co pending application No. 10/839,023, upon allowance of the '023 application, Applicants will consider submitting a terminal disclaimer in compliance with 37 C.F.R. 1.321(b) and (c), if appropriate, which will obviate the rejection.

Rejection of Claims 1-5, 11-13, 16, 18, 19, 82, 140-146, 148 and 154 under 35 U.S.C. §103 (a)

Claims 1-5, 11-13, 16, 18, 19, 140-146, 148 and 154 are rejected under 35 U.S.C. §103 (a) as being unpatentable over Barden *et al.*, "Glycylcyclines 3. 9-Aminodoxycyclinecarboxamides," *J. Med. Chem.*, 37(20):3205-11 (1994).

Claims 1 and 140 and their dependent claims are directed to substituted tetracycline compounds of the formula:



(I)

wherein:

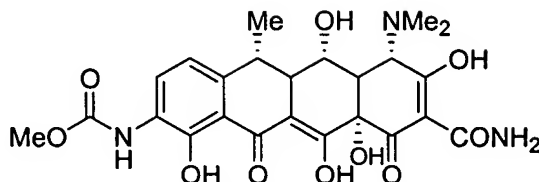
R^9 is $NR^{9c}C(=Z')ZR^{9a}$;

Z is O;

Z' is O or S;

R^{9a} is unsubstituted C_3 - C_{10} alkyl, substituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkylthio, substituted or unsubstituted alkylsulfinyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted arylcarbonyl, substituted or unsubstituted alkylamino, substituted or unsubstituted arylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclic, substituted or unsubstituted heteroaromatic, wherein said substituted alkyl is substituted with halogen, amino, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxycarbonyl, arylcarbonyloxy, alkoxycarbonylamino, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkylaminoacarbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, arylalkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, silyl, aminocarbonyl, alkylthiocarbonyl, phosphate, aralkyl, phosphonato, phosphinato, cyano, acylamino, amido, imino, sulfhydryl, alkylthio, sulfate, arylthio, thiocarboxylate, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl or heteroaryl; further wherein said substituted alkenyl, substituted alkynyl, substituted alkoxy, substituted alkylthio, substituted alkylsulfinyl, substituted alkylsulfonyl, substituted arylsulfonyl, substituted alkoxycarbonyl, substituted arylcarbonyl, substituted alkylamino, substituted arylalkyl, substituted aryl, substituted heterocyclic, or substituted heteroaromatic is substituted with halogen, amino, alkyl, alkenyl, alkynyl, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxycarbonyl, arylcarbonyloxy, alkoxycarbonylamino, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkylaminoacarbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, arylalkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, silyl, aminocarbonyl, alkylthiocarbonyl, phosphate, aralkyl, phosphonato, phosphinato, cyano, acylamino, amido, imino, sulfhydryl, alkylthio, sulfate, arylthio, thiocarboxylate, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl or heteroaryl. Claims 82 and 154 are directed to pharmaceutical compositions comprising the compounds of formula (I).

In contrast, Barden *et al.* describes a compound of the formula:



The Examiner asserts that “[t]he instant claimed compounds would have been obvious [over Barden *et al.*] because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference.” In addition, the Examiner states that since Barden *et al.* alleges that the potency of the compounds increased with additional alkyl groups on the amide chain, “one of ordinary skill in the art would be motivated to prepare compounds with larger groups bonded to the oxygen as well.”

Applicants respectfully disagree. A skilled artisan would appreciate that even small modifications in chemical structure can effect the pharmacological activity, and therefore, even if the prior art teaches a methyl ester, a skilled artisan would not reasonably know that the ethyl ester would have similar pharmacological activity.

However, in the interest of expediting prosecution, Applicants’ have amended the claims removing the terms “absent or prodrug moiety” from the definition of R^{9a}. Barden *et al.* neither teaches nor suggests the use of substituted alkyl groups or the other R^{9a} groups claimed by Applicants.

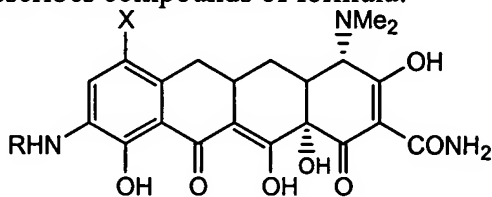
Applicants respectfully submit that the claims, as amended, are non-obvious over Barden *et al.* and request that this rejection of claims 1-5, 11-13, 16, 18, 19, 140-146, 148 and under 35 U.S.C. §103 (a) be withdrawn.

Rejection of Claims 140-146, 148-150 and 154 under 35 U.S.C. § 102(b)

Claims 140-146, 148-150 and 154 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hlavka *et al.*, U.S. Patent 5,494,903. Applicants respectfully traverse this rejection.

As described above, Applicants’ claims 140 and 154 and their dependent claims are directed to tetracycline compounds of formula (I).

In contrast, Hlavka *et al.* describes compounds of formula:



wherein R is R⁴(CH₂)_nCO- and n = 0.

Hlavka *et al.* only describes compounds wherein the R (e.g., the substituent which corresponds to Applicants' $C(=Z')ZR^{9a}$ is a C_1 - C_4 alkoxy carbonyl. Hlavka *et al.* does not teach or suggest tetracycline compounds of the above formula where R is $C(=Z')ZR^{9a}$, Z is O, Z' is O or S and R^{9a} is unsubstituted or substituted C_5 - C_{10} alkyl or any of the other R^{9a} groups claimed by Applicants.

Therefore, Applicants respectfully request that this rejection of claims 140-146, 148-150 and 154 under 35 U.S.C. §102(b), be withdrawn.

Rejection of Claim 139 under 35 U.S.C. §112, second paragraph

Claim 139 is rejected under 35 U.S.C. §112, second paragraph as being indefinite. In particular, the Examiner notes that "there is no way to determine the meets and bounds of a claim generically defined as a "substituted" compound."

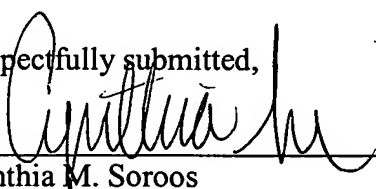
Applicants disagree. However, in the interest of expediting prosecution of the application, Applicants have amended claim 139 removing the term "substituted."

Therefore, Applicants respectfully submit that this rejection of the claims under 35 U.S.C. § 112, second paragraph, no longer applies to the claim as amended, and respectfully request that it be withdrawn.

SUMMARY

It is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conference with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

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Respectfully submitted,

By
Cynthia M. Soroos
Registration No.: 53,623
LAHIVE & COCKFIELD, LLP
One Post Office Square
Boston, Massachusetts 02109-2127
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicant